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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,427	12/05/2003	Kevin J. Tracey	3268.1005-001	8405

21005 7590 06/08/2005

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EXAMINER	
GRAFFEO, MICHELLE	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 06/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/729,427	TRACEY ET AL.	
	Examiner	Art Unit	
	Michelle Graffeo	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4, 10-15 and 20-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,10-15 and 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/17;5/26;*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-24, drawn to a method of mediating a proinflammatory cytokine comprising: a spiro-azabicyclic compound (claims 1-6 and 20-24), classified in class 514, subclass 278; a spiroazabicyclic heterocyclic compound (claims 1-4, 7-9 and 20-24), classified in class 514, subclass 233.2; an anabaseine derivative (claims 1-4, 10-15 and 20-24), classified in class 514, subclass 334; a tropane (claims 1-4, 16-18 and 20-24), classified in class 514, subclass 304; and a quaternary analog of cocaine (claims 1-4, 19 and 20-24), classified in class 514, subclass 212.01.

II. Claims 25-34, drawn to a method for determining whether a compound is a cholinergic agonist, classified in class 514, subclass 1.

III. Claims 35-48, drawn to a method for determining whether a compound is a cholinergic antagonist, classified in class 514, subclass 1.

IV. Claims 49-55, drawn to an oligonucleotide and a method of inhibiting attenuation of TNF release comprising an oligonucleotide, classified in class 435, subclass 6.

The inventions are either independent or distinct from each other.

Group I is patentably distinct from Groups II and III. Inventions are distinct if it can be shown that they are not disclosed as capable of use together and/or have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions do not *per se* require the particulars of each other for their practice. A method of mediating a proinflammatory cytokine does not require a method of determining whether a compound is a cholinergic agonist nor does a method of treatment require *per se* determining whether or not the compound/composition is an agonist or antagonist. The former is directed to a treatment and the later to methods of identifying the function of a compound.

Groups II and III are distinct because the end result of the test process of each group identifies a different compound with opposite functions. One is an agonist while the other is an antagonist. In addition, Groups II and III are distinct from that that of Group IV since a method of determining whether a compound is an agonist or antagonist would not have been used nor result in the oligonucleotide nor the Group IV process of using an oligonucleotide.

Groups I and IV are directed to methods of mediating a proinflammatory cytokine comprising structurally dissimilar compounds. The compounds of Group I are nonnucleotide/nonpeptide organic compounds while Group IV employs a nucleic acid fragment.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

Should Applicant elect Group I, Applicant is required under 35 U.S.C. 121 to elect a single disclosed compound for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claim 1 is generic.

Group I contains a number of compounds for practice of methods of treatment each of which includes a compound and a disorder to be treated. Applicant must elect a compound from the following:

- a spiro-azabicyclic compound,
- a spiroazabicyclic heterocyclic compound,
- an anabaseine derivative,
- a tropane, or
- a quaternary analog of cocaine

As for the above five (5) different classes of compounds, each is patentably distinct and/or independent, one from the other. For example, the tropane is searched and classified in Class 514, subclass 304 whereas cocaine is classified in Class 514, subclass 212.01.

In addition, applicant needs to elect one class of disorders from A through T and where the class has more than one disease, one disease from the class of diseases from the following:

A. an inflammatory condition (appendicitis, peritonitis, pancreatitis, epiglottitis, cholangitis, cholecystitis, asthma, hepatitis, epididymitis, vaginitis, prostatitis, urethritis, bronchitis, rhinitis, pneumonitis, alvealitis, bronchiolitis, pharyngitis, pleurisy, sinusitis, vasculitis, angiitis, endocarditis, arteritis, thrombophlebitis, pericarditis, myocarditis, periarteritis nodosa, neuritis, uveitis, artritides, osteomyelitis, fasciitis, rheumatoid arthritis, arthritides, synovitis, thyroiditis, Goodpasture's syndrome, Behcet's syndrome, and ankylosing spondylitis);

B. a disease caused by a viral agent (influenza, respiratory syncytial virus infection, herpes infection, HIV infection, hepatitis B virus infection, hepatitis C virus infection and Dengue fever);

C. a disease caused by agents other than viral and/or viral(ulcers, hepatitis, Whipple's disease, sepsis, septicemia, disseminated bacteremia, candidiasis, malaria, filariasis, amebiasis, meningitis, encephalitis, periodontal disease and pneumoultramicroscopic silicovolcanoconiosis);

D. an immunoregulatory disease (allergy, anaphylactic shock, immune complex disease, hay fever, endotoxic shock, septic abortion, systemic lupus erythematous, allograft rejection and graft-versus-host disease);

E. achalasia;

F. cardiovascular disorder (organ ischemia, reperfusion injury, myocardial ischemia and congestive heart failure);

G. organ necrosis;

H. cachexia;

I. hyperpyrexia;

J. eosiniphilic granuloma, granulomatosis and sarcoidosis;

K. emphysema, chronic obstructive pulmonary disease and adult respiratory distress syndrome;

L. hydatid cysts;

M. burns;

N. atherosclerosis;

O. coeliac disease;

P. spinal chord injury and paralysis;

Q. arthralgias;

R. Paget's disease; gout;

S. Beger's disease; or

T. Hodgkins disease.

In each of the above, the disease classes are patentably distinct as to the disease symptomology, treatment, expected outcome, and, for example, the patient population. The search for the compounds and treatment of any one disease is not readily expected to have resulted in a complete search of the relevant patent and non

patent literature for any one other invention. In this instance, and for example, treatment for anaphylactic shock differs from treatment for paralysis.

Applicant is advised that a reply to this requirement must include an identification of the class and disease elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the classes of disease and/or diseases are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing them to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with Steve Davis on April 28, 2005 a provisional election was made with traverse to prosecute the invention of Group I drawn to an anabaseine derivative for treating rheumatoid arthritis, claims 1-4, 10-15 and 20-23. Claims 1-4, 10-15 and 20-23 are therefore pending and examined. Affirmation of this

election must be made by applicant in replying to this Office action. Claims 5-9, 16-19 and 24-55 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 10-15 and 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borovikova et al. Vagus nerve stimulation attenuates the systemic inflammatory response to endotoxin. Letter to Nature 2000; 405:458-462 in view of Moreland et al. Treatment of Rheumatoid Arthritis with a Recombinant Human Tumor Necrosis Factor Receptor (p75)-Fc Fusion Protein. The New England Journal of

Medicine 1997:337: 141-147 and further in view of US Patent Number 5,977,144 to Meyer et al.

Borovikova et al. teach that the α-bungarotoxin-sensitive nicotinic acetylcholine receptors (see Meyer et al. below which teach that the α-7 nicotinic receptors were in fact α-bungarotoxin-sensitive nicotinic acetylcholine receptors) are required for inhibition of tumor necrosis factor (TNF) and that these receptors mediate the TNF response in macrophages (see page 459 second column and page 461 first column).

Borovikova et al. do not teach that an anabaseine derivative can be used to agonize the receptor and subsequently treat rheumatoid arthritis (RA).

Moreland et al. teach that TNF plays a role in the pathogenesis of RA (see page 141 col 2) and suggests that a reduction of TNF may reduce the activity of RA (see Abstract background).

Meyer et al. teach that anabaseine derivatives and in particular that 3-(4-hydroxy-2-methoxybenzylidene) anabaseine (see col 5 line 4) and 3-(2,4-dimethoxybenzylidene) anabaseine (see col 1 line 46) selectively target the α-7 nicotinic receptor (see col 3 lines 48-58 and the Abstract) and that the α-7 nicotinic receptors are in fact α-bungarotoxin-sensitive nicotinic acetylcholine receptors (see col 1 lines 38-45).

One skilled in the art is motivated to combine the above references. The advantages of each reference as combined is directed to the teaching of treating RA with an anabaseine compound via the modulation of TNF. Specifically, Moreland et al. teach that modulation of TNF can treat RA and that interference with the cytokine cascade may be of additional benefit in treating RA (see page 146 2nd column).

Therefore, one skilled in the art would be motivated to look to the mechanisms by which one can modulated TNF. Borovikova et al. teach that TNF synthesis can be inhibited (see page 458 col 2) by direct stimulation of the vagus nerve, which is analogous to an increase of acetylcholine. Borovikova et al. also teach that a decrease in TNF is further known to be effected via the α-bungarotoxin-sensitive nicotinic acetylcholine receptor pathway. Moreover both Moreland et al. and Borovikova et al. address the issue of inflammation (see col 2 in Moreland and page 459 col 2 in Borovikova et al.), a common symptom of RA, and the role of TNF therein. One skilled in the art would be further motivated to combine Meyer et al. with Borovikova et al. since one skilled in the art looking to agonize the α-7 receptor would be motivated to look to popular and known α-7 receptor agonists such as those described in Meyer et al. Thus, the claimed invention of the composition was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

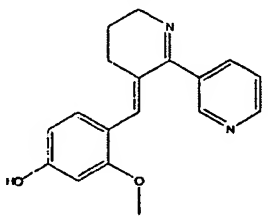
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

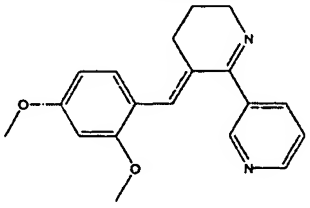
Claims 1-4, 10-15 and 20-23 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 11-14 and 18 of U.S. Patent No. 6,838,471 to Tracey in view of US Patent No. 5,977,144 to Meyer et al. since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows in the comparison table below:

Claims of 10/729427	Claim limitations of '427	Claim limitations in US 6,838,471 reference
1	A method of treating a patient with an anabaseine derivative selective for an α-7 nicotinic receptor to decrease the amount of proinflammatory cytokine that is released from a macrophage wherein the condition is RA.	Claim 5: A method for inhibiting the release of a proinflammatory cytokine from a cell in a patient suffering from a condition mediated by an inflammatory cytokine comprising treating the cell with an agonist* selective for the α-bungarotoxin-sensitive nicotinic acetylcholine receptor to decrease the amount of proinflammatory cytokine wherein the cell is a macrophage to the extent that the condition is RA. See Meyer et al. at col 1 lines 35-42 which teaches that the α-bungarotoxin-sensitive nicotinic acetylcholine receptor is the α-7 nicotinic receptor. See also claims 1-4, 6-8, 11-14 and 18.
2	A method of treating a patient	Claim 3: A method for inhibiting

	with an anabaseine derivative selective for an α-7 nicotinic receptor to decrease the amount of proinflammatory cytokine, such as TNF for example, that is released from a macrophage wherein the condition is RA.	the release of TNF from a cell to the extent that cell is in a patient, comprising treating the cell with an agonist selective for the α-bungarotoxin-sensitive nicotinic acetylcholine receptor to decrease the amount of proinflammatory cytokine wherein the cell is a macrophage to the extent that the condition is RA. See also claims 1, 2, 4-8 and 11-14 and 18.
3	A method of treating a patient with an anabaseine derivative selective for an α-7 nicotinic receptor to decrease the amount of TNF that is released from a macrophage wherein the condition is RA.	Claim 3: A method for inhibiting the release of TNF from a cell to the extent that cell is in a patient, comprising treating the cell with an agonist selective for the α-bungarotoxin-sensitive nicotinic acetylcholine receptor to decrease the amount of proinflammatory cytokine wherein the cell is a macrophage to the extent that the condition is RA. See also claims 1, 5-8 and 11-14 and 18.
4	Same as claim 1	
10	Same as claim 1	
11	A method of treating a patient with certain anabaseine derivatives selective for an α-7 nicotinic receptor to decrease the amount of proinflammatory cytokine that is released from a macrophage wherein the condition is RA.	Claim 5: A method for inhibiting the release of a proinflammatory cytokine from a cell in a patient suffering from a condition mediated by an inflammatory cytokine comprising treating the cell with an agonist* selective for the α-bungarotoxin-sensitive nicotinic acetylcholine receptor to decrease the amount of proinflammatory cytokine wherein the cell is a macrophage to the extent that the condition is RA. See also claims 1-4, 6-8, 11-14

		and 18
12	A method of treating a patient with certain anabaseine derivatives selective for an α-7 nicotinic receptor to decrease the amount of proinflammatory cytokine that is released from a macrophage wherein the condition is RA.	Claim 5: A method for inhibiting the release of a proinflammatory cytokine from a cell in a patient suffering from a condition mediated by an inflammatory cytokine comprising treating the cell with an agonist* selective for the α-bungarotoxin-sensitive nicotinic acetylcholine receptor to decrease the amount of proinflammatory cytokine wherein the cell is a macrophage to the extent that the condition is RA. See also claims 1-4, 6-8, 11-14 and 18
13	A method of treating a patient with certain anabaseine derivatives selective for an α-7 nicotinic receptor to decrease the amount of proinflammatory cytokine that is released from a macrophage wherein the condition is RA.	Claim 5: A method for inhibiting the release of a proinflammatory cytokine from a cell in a patient suffering from a condition mediated by an inflammatory cytokine comprising treating the cell with an agonist* selective for the α-bungarotoxin-sensitive nicotinic acetylcholine receptor to decrease the amount of proinflammatory cytokine wherein the cell is a macrophage to the extent that the condition is RA. See also claims 1-4, 6-8, 11-14 and 18
14	A method of treating a patient with the anabasein derivative:  (VI). selective for an α-7 nicotinic receptor to decrease the amount	Claim 5: A method for inhibiting the release of a proinflammatory cytokine from a cell in a patient suffering from a condition mediated by an inflammatory cytokine comprising treating the cell with an agonist* selective for the α-bungarotoxin-sensitive nicotinic acetylcholine receptor to decrease the amount of proinflammatory cytokine

	of proinflammatory cytokine that is released from a macrophage wherein the condition is RA.	wherein the cell is a macrophage to the extent that the condition is RA. See also claims 1-4, 6-8, 11-14 and 18
15	A method of treating a patient with the anabaseine derivative:  (V). selective for an α-7 nicotinic receptor to decrease the amount of proinflammatory cytokine that is released from a macrophage wherein the condition is RA.	Claim 5: A method for inhibiting the release of a proinflammatory cytokine from a cell in a patient suffering from a condition mediated by an inflammatory cytokine comprising treating the cell with an agonist* selective for the α-bungarotoxin-sensitive nicotinic acetylcholine receptor to decrease the amount of proinflammatory cytokine wherein the cell is a macrophage to the extent that the condition is RA. See also claims 1-4, 6-8, 11-14 and 18
20	Same as Claim 1	
21	Same as Claim 1	
22	Same as Claim 1	
23	Same as Claim 1	

* See US 5977144 to Meyer et al. which teaches anabaseine derivatives as α-7 nicotinic receptor agonists. Particular anabaseine derivatives include those of claims 13 and 14 above. It would be obvious to one skilled in the art to combine Meyer et al. with the '471 reference. Both are directed to the targeting of the α-7 receptors and one skilled in the art would find it obvious to use the well studied agonists of Meyer et al.

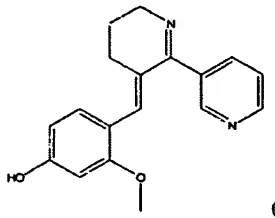
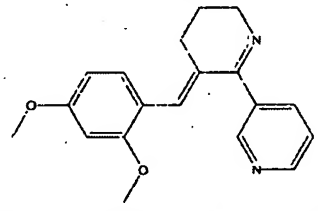
Claims 1-4, 10-15 and 20-23 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 5-6, 14 and 16 of U.S. Patent No. 6,610,713 to Tracey in view of US Patent No. 5,977,144 to Meyer

et al. since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows in the comparison table below:

Claims of 10/729427	Claim limitations of '427	Claim limitations in US 6,610,713 reference
1	A method of treating a patient with an anabaseine derivative selective for an α-7 nicotinic receptor to decrease the amount of proinflammatory cytokine that is released from a macrophage wherein the condition is RA.	Claim 5: A method for inhibiting the release of a proinflammatory cytokine from a cell in a patient suffering from a condition mediated by an inflammatory cytokine comprising treating the cell with a cholinergic agonist* to decrease the amount of proinflammatory cytokine wherein the cell is a macrophage and to the extent that the condition is RA. See also claims 1-3, 6, 14 and 16.
2	A method of treating a patient with an anabaseine derivative selective for an α-7 nicotinic receptor to decrease the amount of proinflammatory cytokine, such as TNF for example, that is released from a macrophage wherein the condition is RA.	Claim 3: A method for inhibiting the release of TNF from a cell to the extent that cell is in a patient, comprising treating the cell with a cholinergic agonist to decrease the amount of proinflammatory cytokine wherein the cell is a macrophage to the extent that the condition is RA. See also claims 1, 2, 5, 6, 14 and 16.
3	A method of treating a patient with an anabaseine derivative selective for an α-7 nicotinic receptor to decrease the amount of TNF that is released from a	Claim 3: A method for inhibiting the release of TNF from a cell to the extent that cell is in a patient, comprising treating the cell with a cholinergic agonist to

	macrophage wherein the condition is RA.	decrease the amount of proinflammatory cytokine wherein the cell is a macrophage to the extent that the condition is RA. See also claims 1, 5, 6, 14 and 16.
4	Same as claim 1	
10	Same as claim 1	
11	A method of treating a patient with certain anabaseine derivatives selective for an α-7 nicotinic receptor to decrease the amount of proinflammatory cytokine that is released from a macrophage wherein the condition is RA.	Claim 5: A method for inhibiting the release of a proinflammatory cytokine from a cell in a patient suffering from a condition mediated by an inflammatory cytokine comprising treating the cell with a cholinergic agonist* to decrease the amount of proinflammatory cytokine wherein the cell is a macrophage to the extent that the condition is RA. See also claims 1-3, 6, 14 and 16.
12	A method of treating a patient with certain anabaseine derivatives selective for an α-7 nicotinic receptor to decrease the amount of proinflammatory cytokine that is released from a macrophage wherein the condition is RA.	Claim 5: A method for inhibiting the release of a proinflammatory cytokine from a cell in a patient suffering from a condition mediated by an inflammatory cytokine comprising treating the cell with a cholinergic agonist* to decrease the amount of proinflammatory cytokine wherein the cell is a macrophage to the extent that the condition is RA. See also claims 1-3, 6, 14 and 16.
13	A method of treating a patient with certain anabaseine derivatives selective for an α-7 nicotinic receptor to decrease the amount of proinflammatory cytokine that is released from a macrophage wherein the	Claim 5: A method for inhibiting the release of a proinflammatory cytokine from a cell in a patient suffering from a condition mediated by an inflammatory cytokine comprising treating the cell with a cholinergic agonist* to

	condition is RA.	decrease the amount of proinflammatory cytokine wherein the cell is a macrophage to the extent that the condition is RA. See also claims 1-3, 6, 14 and 16.
14	A method of treating a patient with the anabasein derivative:  (VI). selective for an α-7 nicotinic receptor to decrease the amount of proinflammatory cytokine that is released from a macrophage wherein the condition is RA.	Claim 5: A method for inhibiting the release of a proinflammatory cytokine from a cell in a patient suffering from a condition mediated by an inflammatory cytokine comprising treating the cell with a cholinergic agonist* to decrease the amount of proinflammatory cytokine wherein the cell is a macrophage to the extent that the condition is RA. See also claims 1-3, 6, 14 and 16.
15	A method of treating a patient with the anabaseine derivative:  (V). selective for an α-7 nicotinic receptor to decrease the amount of proinflammatory cytokine that is released from a macrophage wherein the condition is RA.	Claim 5: A method for inhibiting the release of a proinflammatory cytokine from a cell in a patient suffering from a condition mediated by an inflammatory cytokine comprising treating the cell with a cholinergic agonist* to decrease the amount of proinflammatory cytokine wherein the cell is a macrophage to the extent that the condition is RA. See also claims 1-3, 6, 14 and 16.
20	Same as Claim 1	
21	Same as Claim 1	
22	Same as Claim 1	
23	Same as Claim 1	

* See US 5977144 to Meyer et al. which teaches the cholinergic agonist anabaseine derivatives as α-7 nicotinic receptor agonists. Particular anabaseine derivatives include

those of claims 13 and 14 above. It would be obvious to one skilled in the art to combine Meyer et al. with the '471 reference. Both are directed to the targeting of the α-7 receptors and one skilled in the art would find it obvious to use the well studied agonists of Meyer et al.

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Graffeo whose telephone number is 571-272-8505. The examiner can normally be reached on 9am to 5:30pm Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

27 May 2005
MG

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